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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,071	02/13/2002	David Bar-Or	4172-3-2	8825
22442	7590	09/24/2004	EXAMINER	
SHERIDAN ROSS PC 1560 BROADWAY SUITE 1200 DENVER, CO 80202				DESAI, ANAND U
		ART UNIT		PAPER NUMBER
		1653		

DATE MAILED: 09/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/076,071	BAR-OR ET AL.
	Examiner Anand U Desai, Ph.D.	Art Unit 1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM  
THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 26 July 2004.
- 2a) This action is **FINAL**.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 531-573 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 531-573 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on 13 February 2002 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:
  1. Certified copies of the priority documents have been received.
  2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>6/18/02, 2/21/03, 9/26/03 &amp; 7/30/04</u>	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election without traverse of Group II, drawn to new amended claims 531-573 in the reply filed on July 26, 2004 is acknowledged. Applicants further elect sequence Asp Ala His Lys (SEQ ID NO:1) as a representative of the sequences claimed in the present application for further examination. Applicants claim that all of the claimed peptides share a common property of binding metal ions, and also share a substantial structural feature of containing a histidine residue at the third amino acid position, thus would be obvious of each other if anyone of the polypeptides is found in the prior art.

### ***Priority***

2. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e). The priority date is the filing date of provisional application 60/157,404, which is October 1, 1999.

### ***Information Disclosure Statement***

3. The information disclosure statements (IDS) submitted on June 18, 2002, February 19, 2003, September 26, 2003 and July 30, 2004 are being considered by the examiner. The citations to Duchette et al. has not been initialed because the web site has been revised on July 15, 2004, and the March 5, 2001 information is not available. The Boggs web site citation was not initialed because the web site was not found. The Bar-Or poster text citation was not initialed because the website, [www.5z.com/aps/](http://www.5z.com/aps/) did not link to a poster section. The "Metal Heads" citation was not initialed because the web link was not found.

***Drawings***

4. The drawings are objected to under 37 CFR 1.83(a) because they fail to show the double bond of imidazole of the histidine amino acid in figure 1 as described in the specification. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

***Claim Objections***

5. Claim 540 is objected to because of the following informalities:
6. Claim 540 describes an amino acid sequence composed of 4 amino acids without a sequence identifier. See MPEP §§ 1.821-1.825, particularly § 1.821(d) When the description or

claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. Appropriate correction is required.

***Specification***

7. The disclosure is objected to because of the following informalities:
8. The CROSS REFERENCE TO RELATED APPLICATIONS section should be updated to include the claim of benefit to provisional application 60/509,045, which was originally filed and given application number 09/816,679.
9. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01. The hyperlinks are on pages 6, 16, and 39, lines 9, 22, 23, and 26, respectively.

Appropriate correction is required.

***Double Patenting***

10. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

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provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

11. Claims 531-573 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 83-118 of copending Application No. 10/186,168. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the current application are drawn to a method of treating an angiogenic disease or condition that includes a neoplastic disease, and the claims of copending application 10/186,168 are drawn to a method of reducing the concentration of a metal in an animal to treat an angiogenic disease or condition that includes a neoplastic disease (see US 2003/0130185 A1, claims 83-118, particularly 83, 113, 115, and 118, current application, claims 531-573).

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### ***Claim Rejections - 35 USC § 112***

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claim 542, 556, 557, 559-562, and 569-573 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. In claim 542, the abbreviation HMS is not clearly defined. Is HMS meant to designate  $\alpha$ -hydroxymethylserine?
15. Claims 556 and 557 are improperly dependent on themselves. It is not clear which claim they should further limit?
16. Claims 556, 557, and 559 further describe variables used to designate the amino acid sequence, but it is not clear how the phrase is interpreted in the alternative? It appears an "or" is missing after the first described variable. For example in claim 559, "...at least one amino acid of  $P_1$ , or at least one amino acid of  $P_2$ , or at least one amino acid of  $P_1$  and at least one amino acid of  $P_2$  is substituted with..."
17. Claims 560-562, and 569-573 are rejected for depending on a rejected claim.

***Claim Rejections - 35 USC § 103***

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

19. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claims 531-573 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blaschuk et al. U.S. Patent 6,610,821 B1 (Effective filing date= July 12, 1996) in view of Sijmons et al. Blaschuk et al. discloses various peptides having the formula P<sub>1</sub>-P<sub>2</sub>, wherein P<sub>1</sub> is: Xaa<sub>1</sub>Xaa<sub>2</sub>His; or Xaa<sub>1</sub>Xaa<sub>2</sub>HisXaa<sub>3</sub>; P<sub>2</sub> is (Xaa<sub>4</sub>)<sub>n</sub>, and Xaa<sub>1-4</sub> are selected from a list of amino acids claimed. For example, Blaschuk et al. discloses SEQ ID NO: 26, which has the following sequence: N-Ac-Cys-Ala-His-Ala-Val-Asp-Cys-NH<sub>2</sub> (see U.S. Patent '821, column 4, lines 5-6). Blaschuk et al. also discloses sequences used to inhibit angiogenesis in a mammal (see U.S. Patent '821, column 5, lines 1-5, column 7, lines 38-42, and column 26, lines 24-57). Claim 531 can be reasonably interpreted as encompassing any peptide as long as the sequence of that peptide falls within the scope of P<sub>1</sub>-P<sub>2</sub> (as defined in the claims). Claim 531 would therefore permit any substituent to be bonded to the  $\alpha$ -amino group of Xaa<sub>1</sub>. If, for example, an acetyl group were bonded to the  $\alpha$ -amino group of Xaa<sub>1</sub>, the sequence of P<sub>1</sub>-P<sub>2</sub> would not be affected. In addition, claim 559, which depends from claim 531 and further limits the peptide formula by describing functional characteristics to a substituent, gives support to the rationale of reasonably interpreting a peptide with substituents. Blaschuk et al. does not disclose the elected SEQ ID NO: 1, Asp-Ala-His-Lys, but applicants remarks to restriction requirement state that all of the claimed peptides share a common property and a structural feature, thus any of the claimed peptides would be obvious of each other if anyone of the polypeptides is found in the prior art.

Sijmons et al. discloses a peptide sequence that is currently being claimed by the formula of claim 531 of the present application. The disclosed sequence is Asp-Ala-His-Lys-Ser-Glu

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(see U.S. Patent '307, SEQ ID NO: 10, sequence list table). It is recognized by a person of ordinary skill in the art that a disclosed protein structure will always produce a function based on structure. Therefore, it would have been obvious to a person having ordinary skill in the art to treat an angiogenic disease or condition in an animal by administering the peptides disclosed in Sijmons et al. in view of the teachings of Blaschuk et al. which disclosed peptides used to inhibit angiogenesis in a mammal (see U.S. Patent '821 as cited above, current application, claims 531-573).

21. Claims 531-573 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshida et al. (Neurosurgery 37(2): 287-293 (1995)) in view of Harford and Sarkar (Acc. Chem. Res. 30: 123-130 (1997)). Yoshida et al. discloses the effects of copper chelation on angiogenesis. Yoshida et al. analyzed tumor weight, and vascular density of rats feed with a copper depletion diet and treated with a copper chelator, D-penicillamine. Yoshida et al. show by histological findings that treated rats have a significantly smaller vascular density compared to a control group of rats (see pp. 289-290, Section on Vascular density and pathological study, Figures 3, and 4). Yoshida et al. demonstrates the inhibition of angiogenesis achieved by chelating copper (see Introduction, pp.287). Yoshida et al. does not disclose the use of the peptide having the formula claimed.

Harford and Sarkar disclose the amino terminal copper and nickel-binding motif found in proteins (see Introduction, pp.123). Harford and Sarkar disclose the binding of copper and nickel to the amino acid sequence Asp-Ala-His, which is the peptide being claimed by the formula in claim 531 (see Figure 3-5, pp. 125). Harford and Sarkar describe the importance of

the Histidine residue being in the 3<sup>rd</sup> position of an amino acid sequence to bind a copper ion (see section on Design of the ATCUN Motif, pp. 126). Harford and Sarkar further disclose the synthetic design of a metal binding site onto a protein, to produce a hybrid protein that is currently being claimed (see Protein Design Utilizing the ATCUN Motif pp. 128, and Conclusion, pp. 130, see current application, claim 531, 542, and 550 in particular).

One would have been motivated to design a metal binding peptide as described in Harford and Sarkar, to chelate copper ions and inhibit angiogenesis as disclosed by Yoshida et al. to treat various angiogenic diseases or conditions, including neoplasms. Therefore, it would have been obvious to a person having ordinary skill in the art to administer a metal binding peptide to treat an angiogenic disease or condition (current application, claims 531-573).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

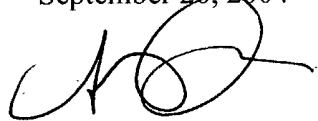
*Karen Cochrane Carlson R.D.*

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A handwritten signature in black ink, appearing to read "M. O.", is positioned below the date.